

In The Specification:

Please delete pages 18-22a as labeled in the amended Specification filed on September 23, 2002 and replace them with the following:

LEGENDS TO FIGURES AND TABLES

Fig. 1:	Flow chart outlining the process of construction of a synthetic human antibody library based on consensus sequences.
<u>Figs. 2A-2G:</u> Fig. 2:	Alignment of consensus sequences designed for each subgroup (amino acid residues are shown with their standard one-letter abbreviation). (A) <u>(2A-2B)</u> (SEQ ID NOS 28-31, respectively) kappa sequences, (B) <u>(2C-2D)</u> (SEQ ID NOS 32-34, respectively) lambda sequences and (C) <u>(2E-2G)</u> (SEQ ID NOS 35-41, respectively), heavy chain sequences. The positions are numbered according to Kabat (1991). In order to maximize homology in the alignment, gaps (-) have been introduced in the sequence at certain positions.
<u>Figs. 3A-3K:</u> Fig. 3:	Gene sequences (SEQ ID NOS 42, 44, 46 and 48, respectively) of the synthetic V kappa consensus genes. The corresponding amino acid sequences (SEQ ID NOS 43, 45, 47 and 49, respectively) (see Fig. 2) <u>(see Fig. 2 Figs. 2A-2B)</u> as well as the unique cleavage sites are also shown.
<u>Figs. 4A-4I:</u> Fig. 4:	Gene sequences (SEQ ID NOS 50, 52 and 54, respectively) of the synthetic V lambda consensus genes. The corresponding amino acid sequences (SEQ ID NOS 51, 53 and 55, respectively) (see Fig. 2) <u>(see Figs. 2C-2D)</u> as well as the unique cleavage sites are also shown.
<u>Figs. 5A-5U:</u> Fig. 5:	Gene sequences (SEQ ID NOS 56, 58, 60, 62, 64, 66 and 68, respectively) of the synthetic V heavy chain consensus genes. The corresponding amino acid sequences (SEQ ID NOS 57, 59, 61, 63, 65, 67 and 69, respectively) (see Fig. 2) <u>(see Figs. 2E-2G)</u> as well as the unique cleavage sites are also shown.
<u>Figs. 6A-6G:</u> Fig. 6:	Oligonucleotides (SEQ ID NOS 70-164, respectively) used for construction of the consensus genes. The oligos are named according to the corresponding consensus gene, e.g., the gene V κ 1 was constructed using the six oligonucleotides O1K1 to O1K6. The oligonucleotides used for synthesizing the genes encoding the constant domains C κ (OCLK1 to 8) and CH1 (OCH1 to 8) are also shown.
<u>Figs. 7A-7D:</u> Fig. 7A/B:	Sequences of the synthetic genes (SEQ ID NOS 165 and 167, respectively) encoding the constant domains C κ (A) <u>(7A-7B)</u> and CH1 (B) <u>(7C-7D)</u> . The corresponding amino acid sequences (SEQ ID NOS 166 and 168, respectively) as well as unique cleavage sites introduced in these genes are also shown.
<u>Figs. 7E-7H:</u>	Functional map and sequence (SEQ ID NOS 169-170, respectively) of

Fig. 7B	module M24 compromising the synthetic C λ gene segment (huCL lambda).
Figs. 7I-7J: Fig. 7C	Oligonucleotides (SEQ ID NOS 171-176, respectively) used for synthesis of module M24.
Figs. 8A-8E: Fig. 8:	Sequence (SEQ ID NOS 177-178, respectively) and restriction map of the synthetic gene encoding the consensus single-chain VH3-V κ 2. The signal sequence (amino acids 1 to 21) was derived from the E. coli phoA gene (Skerra & Pluckthun, 1988). Between the phoA signal sequence and the VH3 domain, a short sequence stretch encoding 4 amino acid residues (amino acid 22 to 25) has been inserted in order to allow detection of the single-chain fragment in Western blot or ELISA using the monoclonal antibody M1 (Knappik & Pluckthun, 1994). The last 6 basepairs of the sequence were introduced for cloning purposes (EcoRI site).
Fig. 9:	Plasmid map of the vector pIG10.3 used for phage display of the H3 κ 2 scFv fragment. The vector is derived from pIG10 and contains the gene for the lac operon repressor, lacI, the artificial operon encoding the H3 κ 2-gene3ss fusion under control of the lac promoter, the lpp terminator of transcription, the single-strand replication origin of the E. coli phage f1 (F1_ORI), a gene encoding β -lactamase (bla) and the ColEI derived origin of replication.
Figs. 10A-10B: Fig. 10:	Sequencing results of independent clones from the initial library, translated into the corresponding amino acid sequences. (A) (SEQ ID NO: 179) Amino acid sequence of the VH3 consensus heavy chain CDR3 (position 93 to 102, Kabat numbering). (B) (SEQ ID NOS 180-191, respectively) Amino acid ssequences of 12 clones of the 10-mer library. (C) (SEQ ID NOS 192-202, respectively) Amino acid sequences of 11 clones of the 15-mer library, *: single base deletion.
Fig. 11:	Expression test of individual library members. (A) Expression of 9 independent clones of the 10-mer library. (B) Expression of 9 independent clones of the 15-mer library. The lane designated with M contains the size marker. Both the gp3-scFv fusion and the scFv monomer are indicated.
Fig. 12:	Enrichment of specific phage antibodies during the panning against FITCBSA. The initial as well as the subsequent fluorescein-specific sub-libraries were panned against the blocking buffer and the ratio of the phage eluted from the FITC-BSA coated well vs. that from the powder milk coated well from each panning round is presented as the "specificity factor".
Fig. 13:	Phage ELISA of 24 independent clones after the third round of panning tested for binding on FITC-BSA.
Fig. 14:	Competition ELISA of selected FITC-BSA binding clones. The ELISA signals (OD.sub.405 nm) of scFv binding without inhibition are taken as

	100%.
Fig. 15:	Sequencing results of the heavy chain CDR3s of independent clones after 3 rounds of panning against FITC-BSA, translated into the corresponding amino acid sequences (SEQ ID NOS 203-218, respectively) (position 93 to 102, Kabat numbering).
Fig. 16:	Coomassie-Blue stained SDS-PAGE of the purified anti-fluorescein scFv fragments: M: molecular weight marker, A: total soluble cell extract after induction, B: fraction of the flow-through, C, D and E: purified scFv fragments 1HA-3E4, 1HA-3E5 and 1HA-3E10, respectively.
Fig. 17:	Enrichment of specific phage antibodies during the panning against β -estradiol-BSA, testosterone-BSA, BSA, ESL-1, interleukin-2, lymphotoxin- β , and LeY-BSA after three rounds of panning.
Fig. 18:	ELISA of selected ESL-1 and .beta.-estradiol binding clones.
Fig. 19:	Selectivity and cross-reactivity of HuCAL antibodies: in the diagonal specific binding of HuCAL antibodies can be seen, off-diagonal signals show non-specific cross-reactivity.
Fig. 20:	Sequencing results of the heavy chain CDR3s of independent clones after 3 rounds of panning against β -estradiol-BSA, translated into the corresponding amino acid sequences (SEQ ID NOS 219-230, respectively) (position 93 to 102, Kabat numbering). One clone is derived from the 10mer library.
Fig. 21:	Sequencing results of the heavy chain CDR3s of independent clones after 3 rounds of panning against testosterone-BSA, translated into the corresponding amino acid sequences (SEQ ID NOS 231-236, respectively) (position 93 to 102, Kabat numbering).
Fig. 22:	Sequencing results of the heavy chain CDR3s of independent clones after 3 rounds of panning against lymphotoxin-.beta., translated into the corresponding amino acid sequences (SEQ ID NOS 237-244, respectively) (position 93 to 102, Kabat numbering). One clone comprises a 14mer CDR, presumably introduced by incomplete coupling of the trinucleotide mixture during oligonucleotide synthesis.
Fig. 23:	Sequencing results of the heavy chain CDR3s of independent clones after 3 rounds of panning against ESL-1, translated into the corresponding amino acid sequences (SEQ ID NOS 245-256 respectively) (position 93 to 102, Kabat numbering). Two clones are derived from the 10mer library. One clone comprises a 16mer CDR, presumably introduced by chain elongation during oligonucleotide synthesis using trinucleotides.
Fig. 24:	Sequencing results of the heavy chain CDR3s of independent clones after 3 rounds of panning against BSA, translated into the corresponding amino acid sequences (SEQ ID NOS 257-262, respectively) (position 93 to 102, Kabat numbering).

<u>Fig. 25A:</u> Fig. 25:	Schematic representation of the modular pCAL vector system.
<u>Figs. 25B-25C:</u> <u>Fig. 25a:</u>	List of restriction sites already used in or suitable for the modular HuCAL genes and pCAL vector system.
<u>Figs. 26A-26D:</u> Fig. 26:	List of the modular vector elements for the pCAL vector series: shown are only those restriction sites which are part of the modular system.
<u>Figs. 27A-27B:</u> Fig. 27:	Functional map and sequence (SEQ ID NO: 263) of the multi-cloning site module (MCS).
<u>Figs. 28A-28G:</u> Fig. 28:	Functional map and sequence (SEQ ID NOS 264-265, respectively) of the pMCS cloning vector series.
<u>Figs. 29A-29B:</u> Fig. 29:	Functional map and sequence (SEQ ID NO: 266) of the pCAL mobile M1 (see Fig. 26) (<u>see Figs. 26A-26D</u>).
<u>Figs. 30A-30C:</u> Fig. 30:	Functional map and sequence (SEQ ID NOS 267-268, respectively) of the pCAL module M7-III (see Fig. 26) (<u>see Figs. 26A-26D</u>).
<u>Figs. 31A-31B:</u> Fig. 31:	Functional map and sequence (SEQ ID NO: 269) of the pCAL module M9-II (see Fig. 26) (<u>see Figs. 26A-26D</u>).
<u>Figs. 32A-32C:</u> Fig. 32:	Functional map and sequence (SEQ ID NO: 270) of the pCAL module M11-II (see Fig. 26) (<u>see Figs. 26A-26D</u>).
<u>Figs. 33A-33D:</u> Fig. 33:	Functional map and sequence (SEQ ID NO: 271) of the pCAL module M14-Ext2 (see Fig. 26) (<u>see Figs. 26A-26D</u>).
<u>Figs. 34A-34D:</u> Fig. 34:	Functional map and sequence (<u>SEQ ID NOS 272-273, respectively</u>) of the pCAL module M17 (see Fig. 26) (<u>see Figs. 26A-26D</u>).
<u>Figs. 35 to 35A-8:</u> 35:	Functional map and sequence (SEQ ID NOS 274-276, respectively) of the modular vector pCAL4.
<u>Figs. 35A-9 to 35A-75:</u> 35a:	Functional map and sequence (SEQ ID NOS 277-300, respectively) of additional pCAL modules (M2, M3, M7I, M7II, M8, M10II, M11II, M12, M13, M19, M20, M21, M41) and of low-copy number plasmid vectors (pCALO1 to pCALO3).
<u>Figs. 35A-76 to 35A-80:</u> 35b:	List of oligonucleotides and primers (SEQ ID NOS 301-360, respectively) used for synthesis of pCAL vector modules.
<u>Figs. 36A-36F:</u> Fig. 36:	Functional map and sequence (SEQ ID NOS 361-362, respectively) of the β -lactamase cassette for replacement of CDRs for CDR library cloning.

<u>Figs. 37A-37D:</u> <u>Fig. 37:</u>	Oligo and primer (SEQ ID NOS 363-367, respectively) design for V κ CDR3 libraries.
<u>Figs. 38A-38D:</u> <u>Fig. 38:</u>	Oligo and primer (SEQ ID NOS 368-371, respectively) design for V λ CDR3 libraries.
Fig. 39:	Functional map of the pBS13 expression vector series.
<u>Figs. 40A-40B:</u> <u>Fig. 40:</u>	Expression of all 49 HuCAL scFvs obtained by combining each of the 7 VH genes with each of the 7 VL genes (pBS13, 30°C.): Values are given for the percentage of soluble vs. insoluble material, the total and the soluble amount compared to the combination H3 κ 2, which was set to 100%. In addition, the corresponding values for the McPC603 scFv are given.
Table 1:	Summary of human immunoglobulin germline sequences used for computing the germline membership of rearranged sequences. (A) kappa sequences, (B) lambda sequences and (C), heavy chain sequences. (1) The germline name used in the various calculations, (2) the references number for the corresponding sequence (see appendix for sequence related citations), (3) the family where each sequence belongs to and (4), the various names found in literature for germline genes with identical amino acid sequences
Table 2:	Rearranged human sequences used for the calculation of consensus sequences. (A) kappa sequences, (B) lambda sequences and (C), heavy chain sequences. The table summarized the name of the sequence (1), the length of the sequence in amino acids (2), the germline family (3) as well as the computed germline counterpart (4). The number of amino acid exchanges between the rearranged sequence and the germline sequence is tabulated in (5), and the percentage of different amino acids is given in (6). Column (7) gives the references number for the corresponding sequence (see appendix for sequence related citations).
Table 3:	Assignment of rearranged V sequences to their germline counterparts. (A) kappa sequences, (B) lambda sequences and (C), heavy chain sequences. The germline genes are tabulated according to their family (1), and the number of rearranged genes found for every germline gene is given in (2).
Table 4:	Computation of the consensus sequence of the rearranged V kappa sequences. (A) (SEQ ID NO: 14), V kappa subgroup 1, (B) (SEQ ID NO: 15), V kappa subgroup 2, (C) (SEQ ID NO: 16), V kappa subgroup 3 and (D) (SEQ ID NO: 17), V kappa subgroup 4. The number of each amino acid found at each position is tabulated together with the statistical analysis of the data. (1) Amino acids are given with their standard one-letter abbreviations (and B means D or N, Z means E or Q and X means any amino acid). The statistical analysis summarizes the number of sequences found at each position (2), the number of occurrences of the most common amino acid (3), the amino acid residue which is most common at this position (4), the relative frequency of the occurrence of the most common amino acid (5) and

	the number of different amino acids found at each position (6).
Table 5:	Computation of the consensus sequence of the rearranged V lambda sequences. (A) (SEQ ID NO: 18), V lambda subgroup 1, (B) (SEQ ID NO: 19), V lambda subgroup 2, and (C) (SEQ ID NO: 20), V lambda subgroup 3. The number of each amino acid found at each position is tabulated together with the statistical analysis of the data. Abbreviations are the same as in Table 4.
Table 6:	Computation of the consensus sequence of the rearranged V heavy chain sequences. (A) (SEQ ID NO: 21), V heavy chain subgroup 1A, (B) (SEQ ID NO: 22), V heavy chain subgroup 1B, (C) (SEQ ID NO: 23), V heavy chain subgroup 2, (D) (SEQ ID NO: 24), V heavy chain subgroup 3, (E) (SEQ ID NO: 25), V heavy chain subgroup 4, (F) (SEQ ID NO: 26), V heavy chain subgroup 5, and (G) (SEQ ID NO: 27), V heavy chain subgroup 6. The number of each amino acid found at each position is tabulated together with the statistical analysis of the data. Abbreviations are the same as in Table 4.

On page 38, as labeled in the original Specification filed on January 24, 2000, in the paragraph beginning at line 4, please amend as follows:

All vector modules were characterized by restriction analysis and sequencing. In the case of module M11-II, sequencing of the module revealed a two-base difference in positions 164/65 compared to the sequence database of the template. These two different bases (CA → GC) created an additional BanII site. Since the same two-base difference occurs in the fl origin of other bacteriophages, it can be assumed that the two-base difference was present in the template and not created by mutagenesis during cloning. This BanII site was removed by site-directed mutagenesis, leading to module M11-III. The BssSI site of module M14 could initially not be removed without impact on the function of the ColE1 origin, therefore M14-Ext2 was used for cloning of the first pCAL vector series. Figures 29 to 34 are showing the functional maps and sequences of the modules used for assembly of the modular vector pCAL4 (see below). The functional maps and sequences of additional modules can be found in Figure 35a Figures 35A-9 to 35A-75. ~~Figure 35b contains a list~~ Figures 35A-76 to 35A-80 contain lists of oligonucleotides and primers used for the synthesis of the modules.

On page 39 as labeled in the original Specification filed on January 24, 2000, in the paragraph beginning at line 3, please amend as follows:

A series of low-copy number plasmid vectors was constructed in a similar way using the p15A module M12 instead of the ColE1 module M14-Ext2. ~~Figure 35a is showing~~ Figures 35A-9 to 35A-75 show the functional maps and sequences of the vectors pCALO1 to pCALO3.